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EXAMINER	
SPIEGLER, A	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/470,944	GUNDLING, GERARD	
	Examiner	Art Unit	
	Alexander H. Spiegler	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *24 January 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. This action is in response to Paper No. 9, filed on January 24, 2001. Currently, claims 1-11, and newly added claims 12-16 are pending. All arguments have been thoroughly reviewed, but are deemed non-persuasive for the reasons which follow. This action is made FINAL. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1 and 5-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Uematsu et al. (EP 0757106 A2, 1997). This rejection now applies to newly added claims 12-14.

Uematsu et al. disclose a method for isolating a nucleic acid by mixing a metal oxide support, a material containing a nucleic acid, and a solution for extracting the nucleic acid forming a sample solution, separating the metal oxide support to which the nucleic acid has been bonded from the sample solution, and eluting the nucleic acid from the magnetic carrier to which the nucleic acid has been bonded (pg. 3, ln. 42-45). Uematsu et al. further teach that the solution used in the extraction of the nucleic acid contains a buffer containing a chaotropic material, such as guanidine salts, potassium iodide, sodium thiocyanate, sodium isothiocyanate, and urea (pg. 5, ln. 54-56). Furthermore, the reference teaches that the buffer can be used in combination with Triton X-100, a known detergent, and Tris HCl buffer (pg. 5, ln.56 - pg.6 ln. 1). With respect to claim 5, the reference further teaches a wash step of an aqueous solution of about 70% ethanol,

following the separation of the metal oxide support/nucleic acid complex from the sample solution (pg.5, 43-44). With respect to claim 6, Uematsu et al. teach that following the wash step the nucleic acid is then eluted form the metal oxide support, with a Tris-EDTA bufer (TE buffer), or sterilized water (pg. 5, ln. 45). With respect to claim 7, the reference further teaches the detection of the nucleic acid after eluting the nucleic acid from the metal oxide support (pg. 3, ln. 57 - pg. 4, ln. 6). With respect to claim 8, the reference further teaches the step of amplifying the eluted nucleic acid (pg. 4, ln. 8-9). With respect to claim 9 and 10, the reference teaches that the nucleic acid used is RNA or DNA, and is taken from a biological source (i.e. whole blood, urine) (pg. 2-3). With respect to claim 11, Uematsu et al. teach a kit for isolating nucleic acid comprising a metal oxide support and a solution for extracting the nucleic acid, which is composed of a chaotropic agent, a detergent, and an elution buffer comprising water (pg. 4, ln. 10-12). With respect to newly added claim 12, the reference teaches (pg. 14, ln. 34-35) teaches the amplification of the nucleic acid without the removal of the elution buffer. With respect to newly added claims 13-14, Uematsu teaches the elution of the nucleic acid can be conducted in a solution having a low ionic strength (for example, sterilized water, which has a pH of 7.0) (pg. 6, ln. 8-9).

The response traverses the rejections made in Paper No. 6, dated September 12, 2000. With respect to the anticipation rejection, applicant traverses the rejection of Uematsu et al. (Claims 1 and 5-11) and states that Uematsu "discloses the use of magnetic-responsive particles that are coated with a substance, and it is the coating that bonds with the nucleic acids", and furthermore, that Uematsu "does not disclose a method of separating nucleic acid from a test sample that comprises the formation of a metal oxide/nucleic acid complex" (pg. 5-6). This

argument is not found to be persuasive for several reasons. First, Applicants are arguing limitations not recited in the claims. The original claims and now the amended claims do not require the limitation that the nucleic acid is bound directly to the metal oxide support. The claims recite "contacting a test sample with a metal oxide support material and a binding buffer to form nucleic acid/metal oxide complexes", whereby there is no specific requirement that the nucleic acid is bound directly to the metal oxide support. Furthermore, the specification does not define the recitation "nucleic acid/metal oxide complex" and therefore does not suggest that the nucleic acid must be bound directly to the metal oxide support. In addition, Uematsu does teach a nucleic acid/metal oxide support (pg. 3, ln. 46), wherein Uematsu recites "separating the magnetic carrier to which the nucleic acid has been bonded from (i.e. nucleic acid/metal oxide complex)". Therefore, applicants arguments are deemed non-persuasive.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Uematsu et al. (EP 0757106 A2, 1997) in view of Koller (US 5128247).

Uematsu et al. disclose a method for isolating a nucleic acid by mixing a metal oxide support, a material containing a nucleic acid, and a solution for extracting the nucleic acid forming a sample solution, separating the metal oxide support to which the nucleic acid has been bonded from the sample solution, and eluting the nucleic acid from the magnetic carrier to which

the nucleic acid has been bonded (pg. 3, ln. 42-45). Uematsu et al. further teach that the solution used in the extraction of the nucleic acid contains a buffer containing a chaotropic material, such as guanidine salts, potassium iodide, sodium thiocyanate, sodium isothiocyanate, and urea (pg. 5). Furthermore, the reference teaches that the buffer can be used in combination with Triton X-100, a known detergent, and Tris HCl buffer (pg. 5, ln.56 - pg.6 ln. 16). Uematsu et al. does not teach the addition of a reducing agent in the buffer used in the extraction of the nucleic acid.

However, Koller teaches of a "nucleic acid releasing composition containing a chaotropic component", which refers to chemical compositions which effectively promote the release of nucleic acids through the disruption and lysis of cells (Col. 3-4). Furthermore, Koller teaches that the nucleic acid releasing component will contain a chaotropic agent, salt, detergent, and a reducing agent (Col. 3-4). Koller (col. 4, ln. 55) teaches that the reducing agent aids in the disruption and lysis of the cells, as well as the disassociation of the proteins from the nucleic acids. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Uematsu by adding a reducing agent to the binding buffer in order to have achieved the benefit stated by Koller of enhancing the extraction and separation of the nucleic acids.

With respect to the obviousness rejection of Uematsu et al. in view of Koller (claim 2), applicant respectfully traverses the rejection and asserts that since claim 2 depends from claim 1, Uematsu does not teach the nucleic acid/metal oxide complex, and Koller is silent with respect to the use of particles to separate nucleic acids from test samples. This argument is deemed non-persuasive for the reasons given above, which points out that Uematsu does teach a nucleic acid/metal oxide complex. Furthermore, it is noted that Koller was not cited for teaching use of

particles to separate nucleic acids from a test sample. Rather, Koller was cited for its teachings that chaotropic compounds, detergents, and reducing agents can be used in conjunction with each other for the separation and isolation of nucleic acids.

6. Claims 2-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uematsu et al. (EP 0757106 A2, 1997) in view of Chomczynski (US 5945515).

The teachings of Uematsu et al. are presented above. In particular, Uematsu et al. teach the isolation of nucleic acids by mixing a metal oxide support, a material containing a nucleic acid, and a solution for extracting the nucleic acid consisting of a buffer containing a chaotropic agent and a detergent, separating the metal oxide support to which the nucleic acid has been bonded from the sample solution, and eluting the nucleic acid from the magnetic carrier to which the nucleic acid has been bonded (p.3-6). Uematsu et al. does not teach a binding buffer further comprising an organic solvent and the flashpoint of the binding buffer is greater than 130 degrees Fahrenheit.

Chomczynski teaches a solution for isolation of RNA, DNA, and proteins from biological material, where the solution comprises a chaotropic agent, detergent, and organic solvent (col. 10, ln. 22-34). With respect to claim 3, Chomczynski teaches that the addition of substantially lower amounts of organic solvents are required to effect the precipitation of cellular components (col. 3, ln.65-68). With respect to claims 2 and 4, Chomczynski further teaches that the solution for the isolation of RNA, DNA, and proteins, also comprises a reducing agent (see abstract, and col. 4 ln. 4). Chomczynski teaches that the reducing agent facilitates denaturation of RNase by the chaotropes and aids in the isolation of undegraded RNA.

In view of the teachings of Chomczynski, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Uematsu et al. so as to have added an organic solvent to a binding buffer comprising a chaotropic agent and a detergent, or a chaotropic agent, detergent, and reducing agent, in order to have achieved the benefit of effecting the precipitation of cellular components. With respect to claims 3 and 4, the resulting binding buffer containing low concentrations of organic solvent effective to precipitate the cellular components would be expected to have a flashpoint of greater than 130^0 F. With respect to claims 2 and 4, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Uematsu by adding a reducing agent to the binding buffer in order to have achieved the advantage stated by Chomczynski of enhancing the denaturation of RNase present in the sample thereby improving the isolation of RNA from the sample.

With respect to the obviousness rejection of Uematsu et al. in view of Chomczynski (claims 2-4), applicant respectfully traverses the rejection and alleges that Chomczynski, like Uematsu does not disclose a method of separating a nucleic acid from a test sample that comprises the formation of a nucleic acid/metal oxide complex. This argument is deemed non-persuasive for the reasons given above. In addition, the applicant traverses the rejection of claim 3, and states "Applicant has examined Chomczynski, but has been unable to identify any explicit teaching or reasonable suggestion that any buffer disclosed therein has a flashpoint of greater that 130^0 F". This argument is deemed non-persuasive since, it would be expected that the binding buffer of Chomczynski would have a flashpoint of at least 130^0 F, since this buffer comprises the same reagents as the buffer set forth in Applicant's specification, wherein the

buffer is characterized therein as having a flashpoint of at least 130^0 F. There is no requirement that Chomczynski disclose the flaashpoint of the buffer, since in the absence of evidence to the contrary, it is a characteristic of the binding buffer of Chomczynski that is has a flashpoint of at least 130^0 F.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS

7. Claims 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uematsu et al. (EP 0757106 A2, 1997), in view of Collins et al. (US 5,750,338).

The teachings of Uematsu are presented above. In particular, Uematsu teaches eluting the bound nucleic acid using, for example, Tris-EDTA buffer (pg. 5, 42-45). The reference does not teach using an elution buffer comprising a sodium phosphate or organophosphate compound.

Collins teaches a method of isolating and amplifying target polynucleotides. Specifically, Collins teaches the method of a target capture assay with a magnetic bead and a target DNA sample (col. 24, ln. 21 to col. 25, ln. 50, Example 1). The reference further teaches the binding of the target nucleic acid to the bead (i.e. forming a nucleic acid/solid support complex) (col. 24, ln. 49-53). Collins further teaches that the bound nucleic acid may be effectively eluted from the bead using a phosphate buffer (col. 24, ln. 53-55). The reference also teaches that the beads may be comprised of metal oxides (col. 11, ln. 18-20).

In view of the teachings of Collins, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Uematsu et al. so as to have used an elution buffer which comprises sodium phosphate in place of TE buffer in order to

have provided an equally effective means for eluting the nucleic acids and providing a suitable medium for storing the eluted nucleic acid.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

9. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alexander H. Spiegler
March 7, 2001

CARLA J. MYERS
PRIMARY EXAMINER